

## Remarks

### Claim amendments:

Claims 2-17 have been amended to properly depend from claim 1.

Claim 10 has been amended to recite an “outer” rather than an “inner” Tn5 recognition element, as present in the original claim.

### Rejection of the claims under 35 USC § 112:

Claims 1-20 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the metes and bounds of the term “extended” are unclear. The claims have been amended to remove the indefinite term. Applicants agree that when comparing two vectors with two different promoters, the expression of one vector may be longer than the other though each may be considered a long period of time. Applicants have amended the claims to obviate the rejection. Amended claims 1 and 18 now claim a process for prolonging expression of a transgene from an expression cassette. Applicants have also amended claims 1 and 18 to provide a clear nexus between forming a linear non-viral DNA vector (containing the expression cassette) and prolonging expression of the transgene. Delivery of the linear DNA vector to the mammalian cell is necessary for the transgene to be expressed. However, the method of delivering the vector to the cell does not affect prolonged expression according to the invention.

Claim 1 has also been amended to incorporate the limitation delivering the linear DNA vector to a mammalian hepatocyte. Support for the amendment can be found in the specification on page 3 lines 21, page 4 lines 1-3, page 4 lines 26-30 and page 7 lines 2-5.

### Rejection of the claims under 35 USC § 102:

Claims 1, 16, 17 and 18 have been rejected under 35 U.S.C. 102(b) as being anticipated by Rolland et al. (US Patent 6,514,947). Applicants respectfully disagree. It is the Applicants opinion that rejection of the claims as being anticipated by Rolland et al. under 102(b) is improper since Rolland et al. was not published or issued more than 1 year prior to the effective filing date of the instant application.

Applicants have submitted with this amendment, a §1.132 Declaration stating conception of delivery of linear DNA to mammalian cells *in vivo* prior to the filing date of the cited prior art. Also submitted with this amendment is a §1.48(a) Request stating that Jon A. Wolff and Vladimir Budker are inventors of the instant application.

Applicants have amended claims 1 and 18 to more clearly set forth their invention. The claims have been amended to claim a process for prolonging expression of a transgene from a given expression cassette by providing the expression cassette on a linear non-viral DNA vector. Delivery of the expression vector is a necessary component for achieving expression of the transgene. However, linearity of the DNA vector, not the method of delivery, prolongs expression of the transgene in the cell. It is the Applicants' opinion that the amended claims provide a clear nexus between forming the linear DNA vector and prolonging expression and that Rolland et al. does not describe a method for prolonging expression of a delivered nucleic acid encoding a transgene.

Claims 1, 5, 7, 18 and 19 have been rejected under 35 U.S.C. 102 (b) as being anticipated by Nabel et al (US Patent 5,733,543). The method of Nabel relies on delivery of the DNA to an immune cell *in vitro* and selection of transfected cells in the antibiotic G-418 before transplanting the cells back into a patient. In contrast, Applicants' claims specify delivery of the non-viral linear DNA vector to mammalian cells *in vivo*. Therefore, it is the Applicants' opinion that Nabel et al. does not anticipate the Applicants' claims.

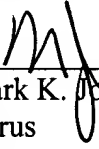
Rejection of the claims under 35 USC § 103:

Claims 1, 7, 14, 15, 18 and 19 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Rolland et al. or Nabel et al. in view of Budker et al. (Gene Therapy 1998). The action states that the inherent property relied upon is not an active step in the claimed method. The action also states that it is not clear if the working example truly represents an unexpected result that can be extended to any polynucleotide. Applicants have amended claims 1 and 18 to make forming the linear DNA vector an active step. In addition to the support provided in the specification for prolonging expression of a

transgene by delivery of a linear vector, subsequent literature in refereed scientific journals supports the Applicants' claim. Chen et al. (IDS reference) have shown that the formation of linear DNA vectors and delivery to hepatocytes *in vivo* provides for prolonged expression of a transgene. The published work by Chen also provides evidence that the claimed method does not rely on the specific sequence disclosed by the Applicant's in their examples, but is generally applicable to other sequences for other expression cassettes and transgenes.

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1-20 should be allowable.

Respectfully submitted,

  
\_\_\_\_\_  
Mark K. Johnson Reg. No. 35,909  
Mirus  
505 South Rosa Road  
Madison, WI 53719  
608-238-4400

I hereby certify that this correspondence is being sent  
by facsimile transmission to: Commissioner for  
Patents, PO Box 1450, Alexandria, VA 22313-1450  
on this date: 6/14/04

  
\_\_\_\_\_  
Kirk Ekena